

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
31 May 2001 (31.05.2001)

PCT

(10) International Publication Number  
**WO 01/38324 A3**

(51) International Patent Classification<sup>7</sup>: C07D 401/04.  
A61K 31/4178. A61P 43/00, C07D 401/14, 417/14,  
409/14, 403/04

[GB/GB]; SmithKline Beecham Pharmaceuticals, New  
Frontiers Science Park South, Third Avenue, Harlow,  
Essex CM19 5AW (GB).

(21) International Application Number: PCT/GB00/04413

(74) Agent: **BLAKEY, Alison, Jane**; SmithKline Beecham,  
Corporate Intellectual Property (CN9.25.1), 980 Great  
West Road, Brentford, Middlesex TW8 9GS (GB).

(22) International Filing Date:

20 November 2000 (20.11.2000)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/166,814	22 November 1999 (22.11.1999)	US
60/166,886	22 November 1999 (22.11.1999)	US
60/166,885	22 November 1999 (22.11.1999)	US
60/166,895	22 November 1999 (22.11.1999)	US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,  
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*):  
**SMITHKLINE BEECHAM P.L.C.** [GB/GB]; New  
Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **DEAN, David,**  
**Kenneth** [GB/GB]; SmithKline Beecham Pharmaceu-  
ticals, New Frontiers Science Park South, Third Avenue,  
Harlow, Essex CM19 5AW (GB). **LOVELL, Peter, John**  
[GB/GB]; SmithKline Beecham Pharmaceuticals, New  
Frontiers Science Park South, Third Avenue, Harlow,  
Essex CM19 5AW (GB). **TAKLE, Andrew, Kenneth**

Published:

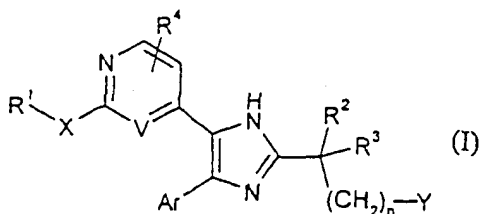
— with international search report

(88) Date of publication of the international search report:  
10 May 2002

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

WO 01/38324 A3

(54) Title: IMIDAZOLE DERIVATIVES AND THEIR USE AS RAF KINASE INHIBITORS



(57) Abstract: Compounds of formula (I) wherein X is O, CH<sub>2</sub>,  
S or NH, or the moiety X-R<sup>1</sup> is hydrogen; V is CH or N; Y is  
NR<sup>10</sup>R<sup>11</sup>, NR<sup>10</sup>C(Z)NR<sup>10</sup>R<sup>11</sup>, NR<sup>10</sup>COOR<sup>11</sup> or NR<sup>10</sup>SO<sub>2</sub>R<sup>11</sup>; Ar is  
phenyl or a 5- or 6-membered heteroaryl ring either of which may  
be optionally substituted; n is 0, 1, 2, 3 or 4; and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>,  
R<sup>10</sup> and R<sup>11</sup> have the meanings given in the description; and phar-  
maceutically acceptable salt thereof.

BEST AVAILABLE COPY

## INTERNATIONAL SEARCH REPORT

Inter. Application No  
PCT/GB 00/04413

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D401/04 A61K31/4178 A61P43/00 C07D401/14 C07D417/14  
C07D409/14 C07D403/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 32436 A (BAYER CORPORATION) 1 July 1999 (1999-07-01) page 2; claim 1 ---	1, 12, 13
A	WO 99 32455 A (BAYER CORPORATION) 1 July 1999 (1999-07-01) page 2; claim 1 ---	1, 12, 13
A	WO 99 01449 A (NOVARTIS AG) 14 January 1999 (1999-01-14) cited in the application page 20; example 18 ---	1, 12
P, A	WO 00 26209 A (NOVARTIS AG) 11 May 2000 (2000-05-11) cited in the application page 28; examples 10, 12-15 --- -/--	1, 12

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

5 June 2001

Date of mailing of the international search report

18/06/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl  
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

## INTERNATIONAL SEARCH REPORT

Inter. Application No

PCT/GB 00/04413

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	WO 99 61437 A (SMITHKLINE BEECHAM CORPORATION) 2 December 1999 (1999-12-02) claims -----	1, 12

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. .nal Application No

PCT/GB 00/04413

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9932436 A	01-07-1999	AU 1905499 A	12-07-1999
		BG 104599 A	30-03-2001
		CN 1283180 T	07-02-2001
		DE 1049664 T	03-05-2001
		EP 1049664 A	08-11-2000
		ES 2153809 T	16-03-2001
		NO 20003230 A	21-08-2000
		TR 200002616 T	21-11-2000
WO 9932455 A	01-07-1999	AU 1905599 A	12-07-1999
		BG 104598 A	28-02-2001
		CN 1283192 T	07-02-2001
		EP 1056725 A	06-12-2000
		ES 2155045 T	01-05-2001
		NO 20003231 A	22-08-2000
		TR 200002617 T	21-11-2000
WO 9901449 A	14-01-1999	AU 8801598 A	25-01-1999
		BR 9810955 A	26-09-2000
		CN 1261885 T	02-08-2000
		EP 0993456 A	19-04-2000
		NO 996429 A	23-12-1999
		PL 337057 A	31-07-2000
		SK 186599 A	12-06-2000
		TR 9903278 T	21-07-2000
WO 0026209 A	11-05-2000	ZA 9805656 A	30-12-1998
WO 9961437 A	02-12-1999	AU 6476599 A	22-05-2000
WO 9961437 A	02-12-1999	AU 4195999 A	13-12-1999
		BR 9910621 A	30-01-2001
		EP 1080087 A	07-03-2001
		NO 20005878 A	21-11-2000